


Breastfeeding: Good for Babies and their Gut Bacteria!

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Canadian Healthy Infant Longitudinal Development (CHILD) Study

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Breastfeeding Rounds – December 9, 2015
Sponsored by the Manitoba Baby Friendly Committee




Objectives

1. Understand how the **microbiome** develops during infancy
2. Identify **factors in early life** that influence microbiome development
3. Describe how **breastfeeding** impacts microbiome development and infant health
4. List key bioactive **components of human milk**
5. Understand that **promoting exclusive breastfeeding during the perinatal period** can positively influence long term breastfeeding duration

Outline

- The CHILD Study
- Gut Microbiome
- Breast Milk: Nature's First Functional Food
- Newborn feeding



CHILD Study Video




AllerGen Whiteboard 3:39

www.canadianchildstudy.ca

The Canadian Healthy Infant Longitudinal Development (CHILD) Study

How do genes and the environment influence child health and development?



www.canadianchildstudy.ca




The Canadian Healthy Infant Longitudinal Development (CHILD) Study

How do genes and the environment influence child health and development?

- **North America's largest general population pregnancy cohort**
3600 children born in 2010 – 2012, four sites in Canada including 1000 in Manitoba
- **Genetic & environmental exposure assessments**
Pregnancy, nutrition, infant feeding, psychosocial, home environment, activities...
- **Biological samples**
Blood, urine, stool, breast milk
- **Follow-up to age 5 years (+)**
Allergies, asthma, obesity...



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CHILD Study

HELP CHILDREN
GROW UP HEALTHY

\$30M Invested
500,000 Biological Samples Banked
200,000 Questionnaires Completed
3600 Families Participating
92% Retention at 3 years (MB)
40+ Senior Researchers
20+ Scientific Disciplines:

Air Quality	Infectious Disease	Physiology
Biostatistics	Molecular Biology	Population Health
Endocrinology	Neonatology	Psychology
Environmental Health	Neuroimmunology	Respirology
Epidemiology	Nutrition	Sociology
Genetics	Obstetrics	Toxicology
Immunology	Pediatrics	Microbiome

MILESTONES

- 5 Year Visit Complete JULY 2018
- 4 Year On Complete JULY 2017
- 3 Year Visit Complete JULY 2016
- 2 Year On Complete JULY 2015
- Infant PPT Visit Complete JULY 2014
- 1 Year Visit Complete JULY 2013
- Home Visit Complete JULY 2013
- Births Complete JULY 2013
- Recruitment Complete JULY 2012

OUTCOMES

- 5 Year Clinical Assessment: Allergy, Sleep, Psychosocial, Environmental Outcomes
- 3 Year Clinical Assessment: Sleep and Neurodevelopment Outcomes
- 1 Year Clinical Assessment: Neurodevelopment, Sleep, Blood, Psychosocial, Microbiome Outcomes
- Birth, Prenatal and Environmental Outcomes
- Baseline Demographics

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Breastfeeding Guidelines

- World Health Organization recommends: **Exclusive breastfeeding up to 6 months of age, with continued breastfeeding along with appropriate complementary foods up to 2 years of age or beyond.**
- USA: most infants initiate breastfeeding, BUT
 - Within 1 week, more than half are receiving formula
 - By 6 months, less than half are breastfed at all
- Canada: most infants (89%) initiate breastfeeding, BUT
 - Only 26% are exclusively breastfed to 6 months
 - Other studies find lower rates...

Sources:
 World Health Organization Global strategy on infant and young child feeding 2002.
 CDC National Immunization Survey 2008. Canadian Community Health Survey 2010-11.

Eight Great Reasons to Breastfeed Your Baby

- It's Convenient** - Breast milk is always quick, clean, the right temperature and available.
- It's Perfect Food For Babies** - Breast milk gives your baby exactly what he or she needs to grow and develop.
- Breastfed Babies Are Healthier** - Breast milk contains antibodies that help a baby have fewer infections and allergies. It is easier to digest so your baby will have less diarrhea and constipation.
- Moms Are Healthier, Too** - Medical research has linked breastfeeding to lowered risk of breast and ovarian cancer.
- Mom Gets Back Into Shape Faster** - Breastfeeding burns extra calories and triggers the uterus to contract and return to its normal shape more quickly.
- It's Better For The Planet** - Breastfeeding is never wasteful. Formula feeding results in discarded cans and bottles.
- Breastfeeding Builds Love** - Skin-to-skin contact brings you and your baby close. It helps your baby feel secure.
- Breastfeeding Saves Money** - Breastfeeding helps the family budget, by saving over \$1000 a year compared to formula.

For more information or support with breastfeeding, contact your local public health nurse, La Leche League or Healthy Baby program.




Breastfed Babies are Healthier...

NOT breastfeeding is associated with **INCREASED** risks of:

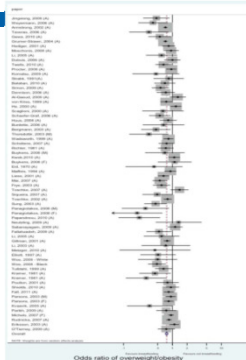
- Infectious disease
 - Diarrhea, respiratory infections, otitis media, UTIs, necrotizing enterocolitis
- Non-infectious disease
 - Type 1 and 2 diabetes, obesity, asthma, allergies, inflammatory bowel disease (IBD)...

Breastfeeding & Obesity


- Meta-analysis of 75 Studies:

10 to 25% reduced risk of obesity in children exposed to longer durations of breastfeeding

(Horta & Victora, WHO 2013)



Breastfeeding & Obesity



Overweight at 1 year:

Breastfeeding	Duration	Adjusted* OR (95%CI)
Breastfeeding at 3 months	None	1.00
	Partial	0.66 (0.37 - 1.19)
	Exclusive	0.36 (0.21 - 0.63)
Breastfeeding at 6 months	None	1.00
	Partial	0.41 (0.26 - 0.65)
	Exclusive	0.18 (0.07 - 0.49)
Breastfeeding Duration	< 6 m	1.00
	6 to < 12 m	0.54 (0.31 - 0.94)
	≥ 12 m	0.26 (0.15 - 0.45)

*Adjusted for birth weight, maternal BM, ethnicity, prenatal smoking and cesarean delivery.

N=849 infants from Manitoba CHILD
 (Azad et al. FASEB J 2014 28:51)

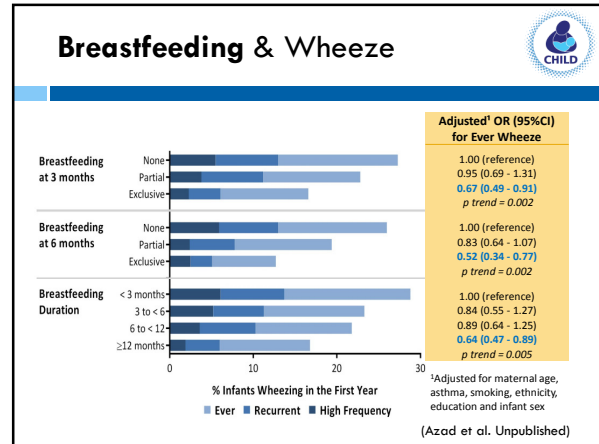
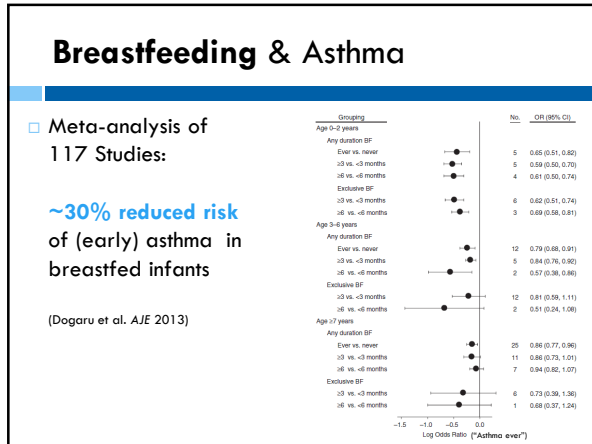
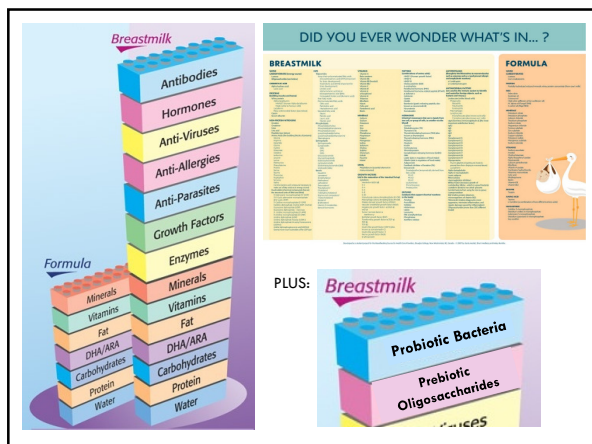


Table 1. Excess Health Risks Associated with Not Breastfeeding

Outcome	Excess Risk* (%)
Among full-term infants	
Acute ear infection (otitis media) ²	100
Eczema (atopic dermatitis) ¹¹	47
Diarrhea and vomiting (gastrointestinal infection) ³	178
Hospitalization for lower respiratory tract diseases in the first year ⁴	257
Asthma, with family history ²	67
Asthma, no family history ²	35
Childhood obesity ⁷	32
Type 2 diabetes mellitus ⁸	64
Acute lymphocytic leukemia ²	23
Acute myelogenous leukemia ²	18
Sudden infant death syndrome ²	56

How?

USDHSS. *The Surgeon General's Call to Action to Support Breastfeeding*. 2011



Human Microbiome

nature CMAJ NEWS

Ten parts bacteria, one part human

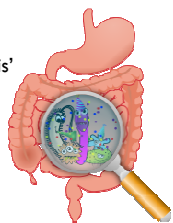
You Are Your Bacteria: How the Gut Microbiome Influences Health

Girth and the Gut (Bacteria)

OUR OTHER GENOME

Gut Microbiota

- ❑ Complex “super organ” of ~ 100 trillion commensal microbes living in the gastrointestinal tract
- ❑ Prevent colonization by pathogens
- ❑ Educate the developing immune system
- ❑ Influence nervous system: ‘gut-brain-axis’
- ❑ Contribute to host metabolism
 - ❑ Digestion of complex carbohydrates
 - ❑ Vitamin production
 - ❑ Energy harvest



The New York Times Magazine

POPULAR SCIENCE

HEALTH


YOUR MICROBIOME MAY HOLD KEYS TO CANCER TREATMENT

THE ANSWER | **The Zoo In You: You Thought You Were Human. But You're Not.**

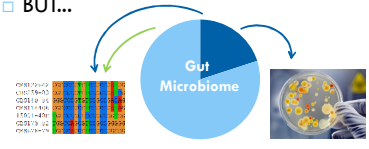
By Alexandra Osso

By JENNIFER HARGREAVES • OCT. 5, 2013

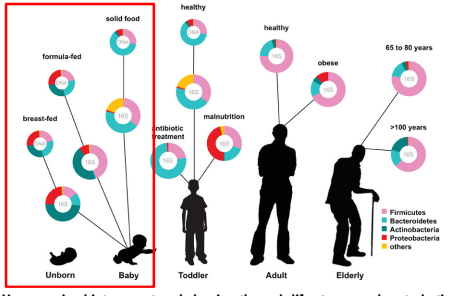
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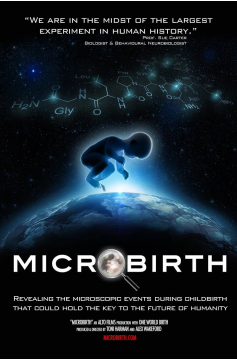
Is this a new idea?

- ❑ No...
 - Clin. Exp. 16, 817-818**
 - Studies on the intestinal flora¹**
 - Part II Bacterial flora of the small intestine in patients with gastrointestinal disorders
 - B. S. DHASAR AND MARGOT SHINER
 - From the Department of Microbiology, High-Prize Institute, St. Mary's Hospital, and The Medical Research Council Gastroenterology Unit, Central Middlesex Hospital, London
 - SUMMARY: The type and distribution of bacteria in the jejunal juice of patients with a variety of gastrointestinal conditions that might affect the small intestine have been examined. Bacterial colonization of the jejunum, defined, in this context, as the occurrence of a bile salt-tolerant flora consisting of both aerobic and anaerobic bacteria resembling that of faeces, was observed only in patients with some form of blind loop. Prominent among the bacteria isolated from these cultured juices were non-spore-forming anaerobic bacteria, most notably Bacteroides, able to hydrolyze bile salts.
- ❑ BUT...
 - 

Gut Microbiota: Dynamic



Human microbiota: onset and shaping through life stages and perturbations.
(Ottman et al. *Front Cell Infect Microbiol* 2012)



Factors influencing mother gut microbiota

- Pregnant weight gain
- Antibiotic exposure
- Hygiene and social condition
- High-fat mother's milk
- Intensive care at birth
- Delivery and feeding modality

Bacteria in amniotic fluid

- Smoking in pregnancy
- Gestational metabolic abnormalities
- Antibiotic exposure
- Weight at birth
- Gestational age

Factors influencing child gut microbiota

Putignani et al. Pediatric Research 2014 76:1

Development of the Gut Microbiome

↑

Increased risk of disease

↓

Health

	Antibiotics			
	Urban environment / overly hygienic lifestyle			
Accumulation of microbes in dysbiotic microbiota	Non-optimal nutrition of the mother	Pre-term birth	Small family size / no pets	
	Cesarean delivery	Formula feeding	Non-optimal nutrition / processed foods	
	Genetic predisposition			
	Prenatal	Birth	Early infancy	Infancy
Accumulation of microbes in normal microbiota	Optimal nutrition of the mother	Vaginal delivery	Breast feeding	Optimal nutrition / fresh foods
	Normal microbiota of the healthy mother	Term birth	Large family size / pets	
	Rural environment / contact with environmental microbes			

(Nylund et al. Proc Natl Acad Sci 2014)

CBC NEWS | Health

Newborns' gut bacteria differ by delivery, breastfeeding

Study suggests how early feeding could explain disease-susceptibility later

Cesarean births and feeding infants formula both shape which bacteria colonize our guts, according to a Canadian study into how those early changes could explain disease susceptibility later in life.

Our bacteria help to digest food, stimulate the development of the immune system, regulate bowels and protect against infection. Doctors and scientists know less about how the microbes take hold early in life and what could disrupt the process.

In Monday's issue of the Canadian Medical Association Journal, researchers in Edmonton, Winnipeg, Toronto and Hamilton said they found infants born by caesarean delivery lacked a group of bacteria common in the stool of infants delivered vaginally, even if they were breastfed.

How a newborn is born could affect what types of bacteria they acquire in their gut (Michael Zeman/Courtesy Christi Carter/Thinkstock/Getty Images)

Decisions regarding C-section delivery will influence the microbiome of the infant.

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External Links

- Out microbiota of healthy Canadian infants, CMAJ
- How delivery mode and feeding can shape bacterial community in infant gut
- Does C/Sc not influence the microbiome?

SCIENCE WORLD REPORT

Baby's Gut Bacteria Determined by Breastfeeding and C-Section

Bruce Squires award for microbiome study

Dr. Anita Kopylov (left) and Dr. Meghan Azad (right), are members of the research team that received the Bruce Squires Award for their study on the gut microbiome of infants.

Mothers W/ CMAJ January 7, 2015

The authors of a study looking at the variability of gut flora in healthy infants with different diet and delivery methods have been awarded for their contribution to health care research in Canada.

Perinatal Exposures & Gut Microbiota

RESEARCH

Gut microbiota of healthy Canadian infants: profiles by mode of delivery and infant diet at 4 months

Meghan B. Azad PhD, Theodore Konya MPH, Heather Maughan PhD, David S. Guttman PhD, Catherine J. Field PhD, Radha S. Chari MD, Malcolm B. Spear MB, Allan B. Becker MD, James A. Scott PhD, Anita S. Kopylov PhD, on behalf of the CHILD Study Investigators

ABSTRACT

Background: The gut microbiota is essential to human health throughout life, yet the acquisition and development of this microbial community during infancy remains poorly understood. Maternal fecal and vaginal colonization over rising rates of caesarean delivery and insufficient exclusive breastfeeding of Canadian infants and the use of formula instead of breast milk have been suggested as factors that may influence the infant gut microbiota. In this article, we characterize the gut microbiota of healthy Canadian infants by mode of delivery and feeding.

Methods: We included a subset of 647 healthy infants from the Canadian Healthy Infant Longitudinal Development (CHILD) birth cohort. Mode of delivery was obtained from medical records, and mother was asked to report on infant diet and breastfeeding. Stool samples were collected at 4 months of age and analyzed for the microbiota composition using high-throughput DNA sequencing.

Results: We observed high profiles of fecal microbes from the phylum Bacteroidetes and the genera Bifidobacterium and Clostridium. There was a significant association between caesarean delivery and infant gut microbiota composition. Infants born by caesarean delivery had significantly lower relative abundance of Bacteroidetes and higher relative abundance of Firmicutes compared with infants born vaginally. Exclusive breastfeeding was associated with higher relative abundance of Bacteroidetes and lower relative abundance of Firmicutes. The association between mode of delivery and infant gut microbiota composition was independent of feeding mode.

Impact of maternal intrapartum antibiotics, method of birth and breastfeeding on gut microbiota during the first year of life: a prospective cohort study

MB Azad, T Konya, H Maughan, D S Guttman, B Chari, C J Field, M B Spear, H Maughan, A B Becker, J A Scott, A S Kopylov, "The CHILD Study Investigators"

Breastfeeding & Microbiota

Breastfeeding favours:
 ↑ Bifidobacteria, ↓ Clostridium difficile, ↓ Diversity...

Prevalence % of Clostridium difficile vs Breastfeeding: None, Partial, Exclusive. p (trend) = 0.01

Relative Abundance (%) of Genus Bifidobacteria vs Breastfeeding Duration (months): Never, <6, 6 to 12, >12. r = 0.365, p < 0.001

(Azad et al. CMAJ 2013, and BJOG 2015)

C-Section, Breastfeeding & Microbiota: 3 Months

Microbiota at 3 months

Microbiota dysbiosis after CS, regardless of feeding

Phyla: Bacteroidetes, Firmicutes, Proteobacteria, Actinobacteria, Verrucomicrobia, Other

(Azad et al. BJOG 2015)

C-Section, Breastfeeding & Microbiota: 1 year

Microbiota at 1 year

Microbiota "recovery" in breastfed infants

Phyla: Bacteroidetes, Firmicutes, Proteobacteria, Actinobacteria, Verrucomicrobia, Other

(Azad et al. BJOG 2015)

Caution: microbiota “recovery”?

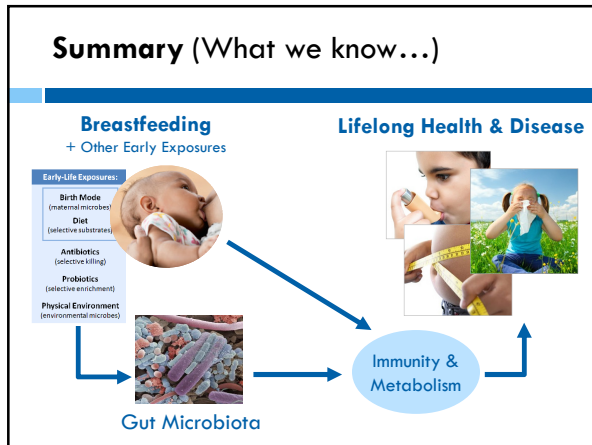
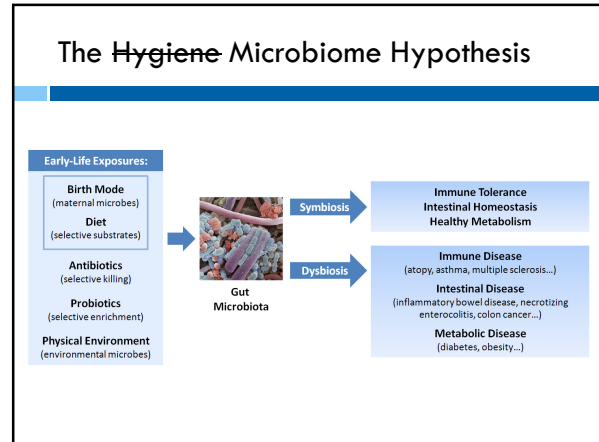
Cell 158, 705–721, August 14, 2014

Cell

Altering the Intestinal Microbiota during a Critical Developmental Window Has Lasting Metabolic Consequences

Laura M. Cox,^{1,2} Shingo Yamashita,² Jiho Sohn,² Alexander V. Alekseyenko,^{2,3} Jacqueline M. Leung,¹ Ilseung Cho,² Sangheon G. Kim,⁴ Hulin Li,² Zhan Gao,² Douglas Mahana,² Jorge G. Zarate Rodriguez,² Arlin B. Rogers,⁵ Nicolas Robine,² Ping Lokke,² and Martin J. Blaser^{1,2,6*}

- Antibiotics used to disrupt microbiota in newborn mice
- Microbiota **recovered** after antibiotic exposure, but immune function and adiposity were **permanently** altered



- ## Future Directions (What we don't know...)
- What does a 'healthy microbiome' look like?
 - What are the **long-term** health effects of microbiota dysbiosis resulting from c-section, antibiotics, formula feeding...?
 - **HOW** do microbiota influence disease risk?
 - How can we **prevent** gut microbiota dysbiosis?
 - Vaginal delivery, **breastfeed**, avoid unnecessary antibiotics...
 - How can we **repair** gut microbiota dysbiosis?
 - Vaginal swabs after CS? **Breastfeed**? Pre/probiotics? Fecal Transplants?

MICROBIOTA

Mother's littlest helpers

Breastmilk nourishes the microbes colonizing the neonatal intestinal tract

By Katie Hilde¹ and Zachary T. Lewis²

Commensal bacteria underlie, in part, our nutritional status, immune function, and psychological well-being. The trillions of beneficial microbes within our intestinal tract convert dietary nutrients, inhibit pathogen colonization, regulate immune processes, and produce neural signals (1, 2). Advances in our understanding of the importance of microbes have motivated the commercial development of products intended to boost “good” commensals and confer health benefits. Probiotic dietary supplements contain live beneficial microbes hoped to substantially colonize the gut. Probiotic nutrients are thought to enhance good gastrointestinal microflora by preferentially nourishing beneficial microbes. From “probiotics” are being explored to ameliorate symptoms of psychiatric illness. These live organisms influence the brain through metabolites and neuroactive compounds in rodent models and preliminary human studies (3). How to most effectively be the landscape architects of our microbial community, however, often remains unclear. An opportunity to gain insights into how natural selection has shaped the coevolution of hosts and microbes can be found in mammalian mother-infant dyads, as our microbiota are ecologically en-

Breastmilk

Probiotic Bacteria

Prebiotic Oligosaccharides

...IFAS

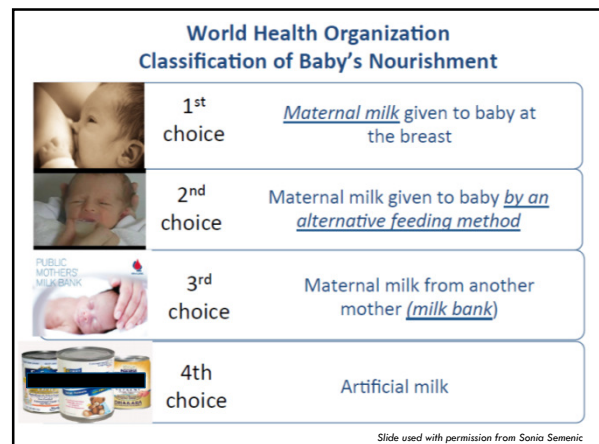
Probiotics:
Live beneficial bacteria

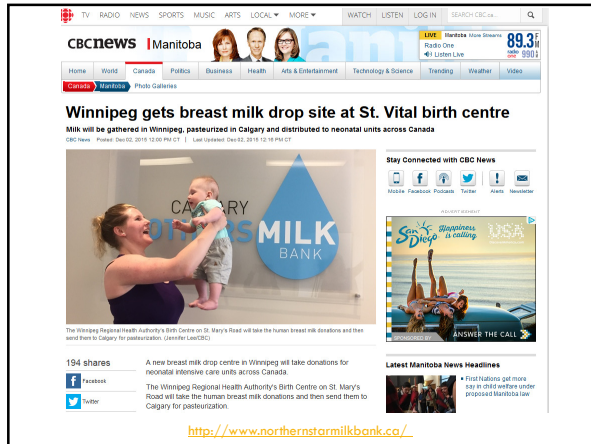
Prebiotics:
Non-digestible carbohydrates that select for beneficial bacteria

...as a result of the intra-oral vacuum dynamics of suckling (4), or via the more speculative translocation to milk through a gastrointestinal route (5, 7).
Once breastmilk is in the intestinal environment of an infant, intense microbial competition exists for both space and nutrients. The major available carbon source, human milk glycom, are complex oligosaccharides and glycosylated compounds that typically pass undigested from the infant stomach because endosymbiont mammals (those with a placental lactase enzyme) to cleave them (6, 8). Investigations of the structure of milk oligosaccharides reveal that human milk has a greater diversity (>200 isomers), more complexity, and higher abundance than the milk of other primates, including all of the great apes (4, 9). Importantly, certain oligosaccharides that dominate human milk, but are absent or rare in other primates, are the preferred food of Bifidobacterium, the most prevalent microbial clade in the healthy infant gut (6).

...our microbiota are ecologically engineered by mothers and breastmilk.

SCIENCE | www.sciencemag.org | 28 JUNE 2015 • VOL 348 | ISSUE 6242 | 1427





Breastfeeding in the CHILD Study

Early intensity predicts long-term duration

Lorena Vehling, BSc (Hons)
University of Manitoba
Children's Hospital Research Institute of Manitoba

Background

Many mother-infant dyads **do not reach** the recommended guidelines of **exclusive breastfeeding for 6 months**

One Canadian study reports only **5% of infants** were still exclusively breastfeeding at 6 months¹

Factors associated with breastfeeding duration include:

- Maternal education
- Method of delivery
- Maternal Ethnicity
- Parity
- Breastfeeding self-efficacy
- Prenatal class attendance
- Maternal health status
- Maternal Intention
- Paternal infant feeding beliefs
- Perceived infant satisfaction
- Postpartum support
- Skin-to-skin care
- In-hospital supplementation**

1. Semenic, S. et al. "Predictors of the duration of exclusive breastfeeding among first-time mothers." *Research in nursing & health* 31.5 (2008): 428-441

OBJECTIVE

To describe and explore associations between breastfeeding initiation, early intensity and duration in a national cohort of Canadian children.

Methods

Cohort of **3141** mother-infant dyads from the CHILD study

Newborn feeding data to determine **breastfeeding status since birth**

- Exclusive (only human breast milk)
- Partial (supplemented with infant formula, other fluids or solid food at any time since birth)
- None

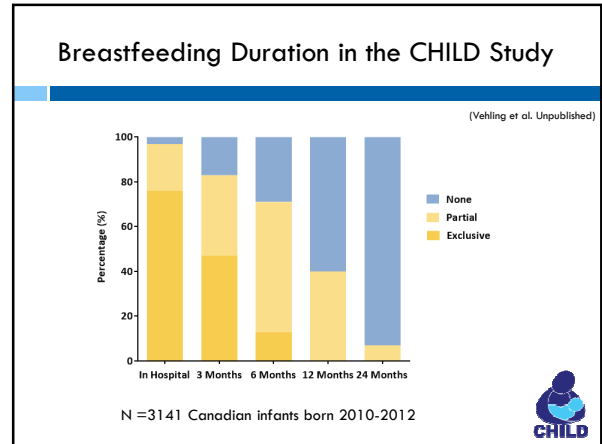
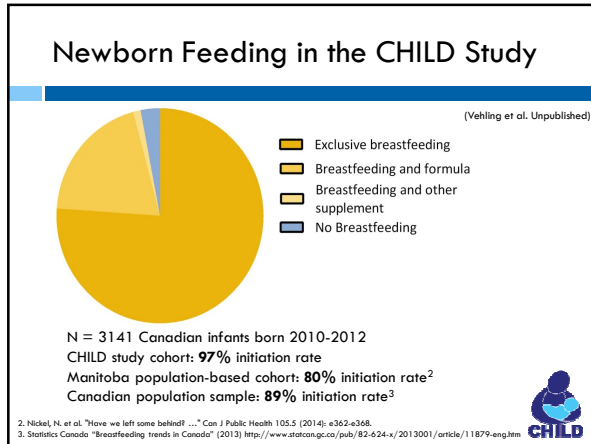
Rate ratios were calculated and associations determined using a **Poisson model**

Fig. 1 CHILD study

Maternal Characteristics in the CHILD Study

	%		%
Maternal Education: Postsecondary Degree		Method of Birth	
Yes	76.4	Vaginal	74.8
No	23.6	Cesarean	25.2
Maternal BMI		Maternal Ethnicity	
Normal	62.4	Caucasian	72.8
Overweight	37.6	Asian	15.8
Parity		First Nations	4.4
Multiparity	53.5	Other	7.0
Primiparity	46.5		

N=2913 children with complete breastfeeding data in the first year, maternal characteristics and were breastfed in hospital.

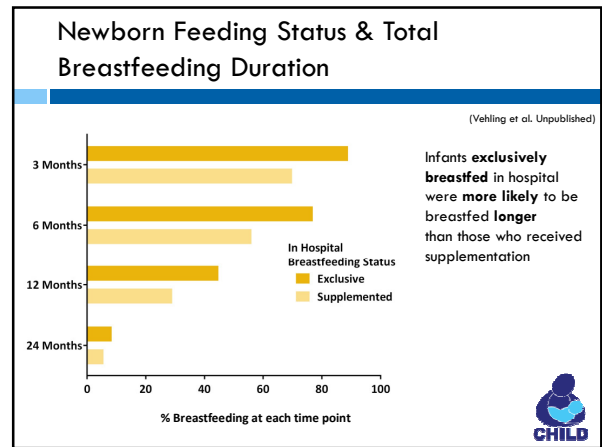
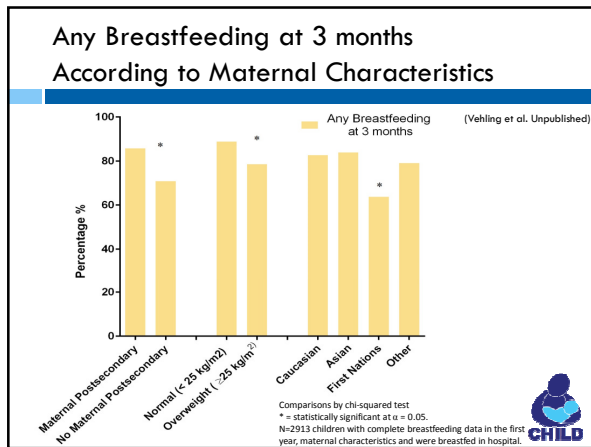
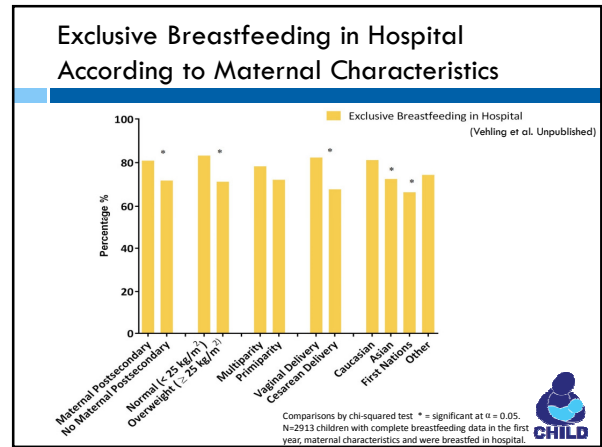


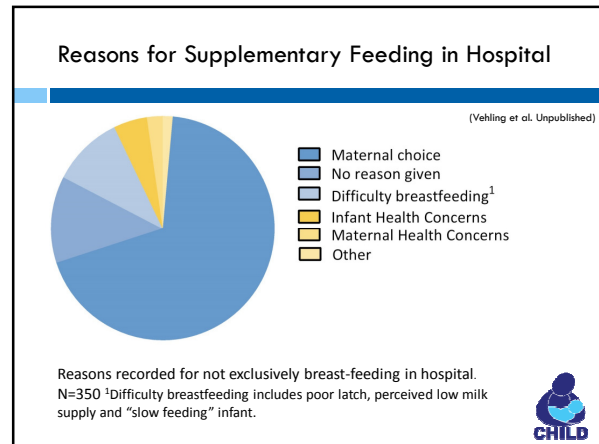
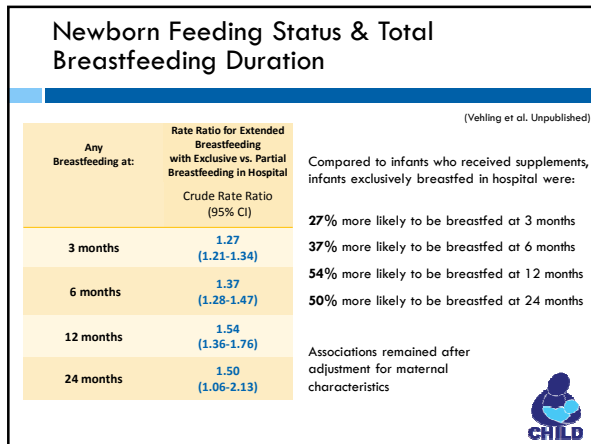
Breastfeeding Across CHILD Study Sites

Study Site	N	Exclusive Breastfeeding in Hospital		Any Breastfeeding at 3 months		Any Breastfeeding at 6 months		Any Breastfeeding at 12 months	
		%	p	%	p	%	p	%	p
Edmonton	721	64.6	ref	82.8	ref	68.8	ref	35.5	ref
Toronto	735	87.3	*	88.4		71.4		34.7	
Vancouver	719	89.2	*	94.7	*	84.4	*	60.5	*
Winnipeg	966	67.7		80.6		70.2		39.9	

"Winnipeg" study site includes children born at:
 - Health Sciences Centre
 - St. Boniface Hospital
 - Boundary Trails


Comparisons by chi-square tests, * = significant results at $\alpha = 0.05$.
 N=3141 children with complete breastfeeding data in the first year including in hospital. (Vehling et al. Unpublished)





Key Finding

Exclusive breastfeeding in hospital is associated with an increased likelihood of extended breastfeeding in the first two years of life.



Ten Steps to Successful Breastfeeding

Step 6: Give newborn infants no food or drink other than breast milk unless medically indicated

Step 4: Help mothers initiate breastfeeding within a half-hour of birth


Step 5: Show mothers how to breastfeed and how to maintain lactation, even if they should be separated from their infants

Breastfeeding Committee for Canada
Comité canadien pour l'allaitement



Previous Research

- Other studies have found that in-hospital supplementation increased early breastfeeding cessation among mothers intending to exclusively breastfeed
- Reasons for supplementing in-hospital has varied widely in other studies including:
 - time of birth
 - maternal fatigue
 - infant behaviour
 - removal of infant to an intensive care area





What's next?

Is there a relationship between common birth interventions/medications and exclusive breastfeeding in hospital?

Are infants born at Baby-Friendly designated hospitals more likely to be breastfed longer?
And are maternal factors as significant?



Is there a relationship between exclusive breastfeeding at 3 or 6 months and long-term duration?


Implications

Baby-friendly initiatives in hospital could have a **long-term impact** on extended breastfeeding rates with significant benefits for **child health and health equity**.

These findings support promotion of **exclusive breastfeeding** in hospital to **new mothers** and **pre- and postnatal health care providers**






Acknowledgements



CHILD Study
Manitoba Team (Site Leader: Allan Becker)



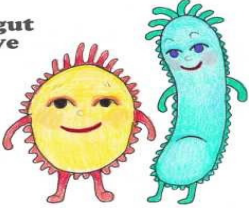





Microbiome Research: SyMBIOTA
Anita Kozyrskyj (Alberta), James Scott (Toronto) & Team

Video

These friendly gut bacteria improve digestion, and help your baby maintain a healthy weight.



Breastfeeding: good for your baby and their gut bacteria! (0:37)
<https://www.youtube.com/watch?v=hGf3E3Kn74k>

CHILD Study Video




Shaw TV 2:14

www.canadianchildstudy.ca